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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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Advisory Action **After the Filing of an Appeal Brief**	**Application No.** 10/578,613	**Applicant(s)** TOHATA ET AL.
	Examiner ILEANA POPA	**Art Unit** 1633

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

The reply filed 18 May 2011 is acknowledged.

1. ☐ The reply filed on or after the date of filing of an appeal brief, but prior to a final decision by the Board of Patent Appeals and Interferences, will not be entered because:

   a. ☐ The amendment is not limited to canceling claims (where the cancellation does not affect the scope of any other pending claims) or rewriting dependent claims into independent form (no limitation of a dependent claim can be excluded in rewriting that claim). See 37 CFR 41.33(b) and (c).

   b. ☐ The affidavit or other evidence is not timely filed before the filing of an appeal brief. See 37 CFR 41.33(d)(2).

2. ☐ The reply is not entered because it was not filed within the two month time period set forth in 37 CFR 41.39(b), 41.50(a)(2), or 41.50(b) (whichever is appropriate). Extensions of time under 37 CFR 1.136(a) are not available.

   Note: This paragraph is for a reply filed in response to one of the following: (a) an examiner's answer that includes a new ground of rejection (37 CFR 41.39(a)(2)); (b) a supplemental examiner's answer written in response to a remand by the Board of Patent Appeals and Interferences for further consideration of rejection (37 CFR 41.50(a)(2)); or (c) a Board of Patent Appeals and Interferences decision that includes a new ground of rejection (37 CFR 41.50(b)).

3. ☒ The reply is entered. An explanation of the status of the claims after entry is below or attached.

4. ☒ Other: *see continuation sheet*

/Ileana Popa/
Primary Examiner, Art Unit 1633

The absence of an example is not evidence for lack of a reasonable expectation of success. Although the appellant refers to Ferrari's Fig. 7 and 8, one would not infer lack of reasonable expectation of success in achieving the claimed invention based on the data presented in these figures. Although the data indicates a slight decrease for some of the deleted mutants at 17 h, these mutants exhibit increased protein production over time, i.e., at 24 and/or 40 h. Thus, the figures demonstrate increased protein production for all tested deleteted mutants. Based on the data in Fig. 7 and 8 and Ferrari's dislcosure, one of skill in the art would have reasonably expected that deleting rocA, D and/or F would also result in increased protein production. While Fig. 7 and 8 indicate variablity with respect to the degree of increase in protein production, the same variablity is encompassed by the instant claims which are drawn to a broad genus of genes to be deleted (as demonstrated by Table 4 on p. 26 of the instant specification).

The argument of unpredictability due to known genetic complexity is not supported by the evidence of record. While it is true that inactivating rocR would inhibit expression of all proteins encoded by the rocABC and rocDEF operons, this is desirable for protein production. Specifically, the prior art teaches that rocR and sigL only control no genes other than the rocABC and rocDEF operons (i.e., no genetic complexity), which operons encode the enzymes necessary for the intracellular arginine catabolism (i.e., degradation) (Gardan et al. cited by the appellant, see p. 826, Fig. 1A; p. 830, column 2, Discussion; Belitsky et al., Proc. Natl. Acad. Sci. USA, 1999, 96: 10290-10295, of record, see p. 10290, column 1, last paragraph and p. 10291, Fig. 1). Based on the teachings in the art as a whole, one of skill in the art would have known that knocking out rocR or sigL would only inhibit rocABC and rocDEF operons (i.e., arginine degradation) and achieve the predictable and desirable result of accumulating arginine within the cell for enhanced protein synthesis.

With respect to the argument of teaching away, there is no teaching in Ferrari that inactivating rocR or sigL renders the method unsatisfactory for protein production. In view of the prior art as a whole and as indicated above, one of skill in the art would have reasonably expected that inactivating rocR or sigL would result in increased protein production.

Finally, the argument of unexpected results obained by deleteing rocR or sigL is not new and was addressed in the Examiner's Answer (it is also noted that the argument is not commensurate in scope with the claims, which are not limited to rocR and sigL but rather recite a broad genus of genes to be deleted). Importantly, based on the teachings in the prior art as a whole, the results obtained by deleting either rocR or sigL are not surprising as one of skill in the art would have expected that inactivating all the genes involved in arginine degradation pathway would result in enhanced yields over the wild type cells.